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EXAMINER	
PANDE, SUCHIRA	
ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,215	ZIMMERMANN ET AL.	
	Examiner	Art Unit	
	Suchira Pande	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-39 and 41-61* is/are pending in the application.

4a) Of the above claim(s) *32-39 and 43-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of method claims 31 and 41-42 in the reply filed on October 25, 2007 is acknowledged. The traversal is on the following ground(s) that:

1) Applicant made an election based upon false information provided by Examiner and

2) Policastro et al. (1986) J. Biol. Chem. 261 (13): PP 5907-5916 teaches sequence of SEQ ID No. 3 but the sequence is still novel according to the Trilateral Exchange Document cited by Applicant.

This is not found persuasive because:

1) The sequence alignment showing 100% match to the claimed SEQ ID no 3 that formed the basis of restriction, was found by STIC during a sequence search, and was provided to Applicant as part of the Office Action mailed on April 26, 2007. Office mistakenly enclosed an earlier Policastro citation with the above indicated office action. That mistake was rectified and with the FAOM the correct Policastro reference was enclosed with appropriate portion of the sequence highlighted. Thus information provided to the Applicant the sequence alignment that forms the basis of restriction requirement was not false.

2) Office does not examine applications based on the Trilateral Exchange Document that is cited by Applicant. Examination of applications by the Office is performed according to MPEP.

Hence the requirement is still deemed proper and is therefore made FINAL.

Claim Status

2. Applicant has cancelled claims 1-30 and 40; amended claims 31, 41 and 42; withdrawn claims 32-39, 43-61. Consequently amended claims 31, 41 and 42 are under consideration and will be examined in this action.

Response to Amendment

Claim Rejections - 35 USC § 112

3. Amendment to claim 31 overcomes the 112 2nd rejection by providing a final process step which clearly relates back to the preamble. Hence this rejection is withdrawn.

4. Amendment to claims 41 and 42 recites methods that do not recite any specific action or step that must be performed or a condition that must be met, so that mRNA detection of at least one of β7-hCG, β6-hCG, and β6e-hCG can be correlated to receptivity of endometrium in actual or subsequent cycle.

The claim in present form does not tell one of ordinary skill in the art under what conditions detection of hCG mRNA can be correlated with optimal endometrial receptivity and under what conditions detection of hCG mRNA can be correlated with non optimal endometrial receptivity. To illustrate this Examiner is giving an example: is there a certain ratio or amount of the β7-hCG, β6-hCG, and β6e-hCG in the sample that indicates optimal conditions for receptivity of endometrium in actual or subsequent cycles while other ratios or amounts of hCG indicate non optimal conditions for receptivity of endometrium in actual or subsequent cycles. Or is it mere detection of β7-hCG, β6-hCG, and β6e-hCG in the sample is indicative of optimal receptivity of

endometrium in actual or subsequent cycle? While non detection of β7-hCG, β6-hCG, and β6e-hCG in the sample is indicative of non optimal receptivity of endometrium in actual or subsequent cycle hCG.

Hence amended claims 41 and 42 in present form are still not clear. Accordingly the 112 2nd rejections of claims 41 and 42 are being maintained.

Response to Arguments

Arguments re 102 rejection of claim 31 and 40 over Bellet et al.

5. Applicant's arguments filed October 25, 2007 have been fully considered but they are not persuasive.

The instant claim is drawn to "----changes in the endometrium or in the epithelium of other organs, the method comprising the steps of :

a) isolating RNA from blood sample or tissue sample----"

Applicant is arguing that cited art Bellet et al. provides no teaching at all in regard to the expression of β7-hCG and β6-hCG in the endometrium.

Examiner would like to indicate that cited art teaches the method comprising the steps of:

a) isolating RNA (see col. 5, lines 35-44 where RNA isolation is taught) from a blood sample or tissue sample (see col. 4, lines 46-53 where wide variety of tissue samples including whole blood are taught);

Therefore by teaching conditions explicitly recited in active first step of instant claim namely isolating RNA from blood Bellet et al. meets the criteria recited in instant claim.

Applicant has amended the base claim 31 by adding the limitation wherein detection of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG indicates receptivity of the endometrium for implantation.

Examiner would like to point out that the cited art Bellet et al. teaches the added limitation namely detection of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG (See col. 4 line 4 where RT-PCR is taught for expression or over expression of mRNA (for detection of CGβ transcripts) of at least one of β7-hCG, β6-hCG, and β6e-hCG (see col. 1, line 43 where β7-hCG and β6-hCG are taught).

Further applicant reiterates in the arguments "When no expression of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG is detected, the endometrium is not receptive". The above statement indicates mere detection of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG indicates that the endometrium is receptive for implantation.

In other words irrespective of the fact whether art cited recognizes or teaches this correlation or not, the detection mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG will be accompanied by the endometrium being receptive at the same time. In other words mRNA expression of β7-hCG, β6-hCG, and β6e-hCG is an inherent property of endometrium that is receptive for implantation.

As the cited art teaches detection of β7-hCG and β6-hCG mRNA from blood therefore the cited art inherently indicates receptivity of the endometrium for implantation.

Therefore the cited art is still applicable to the amended claim. Hence the 102 (b) rejection is being maintained.

Arguments re 103 rejection of claim 41 and 42 over Bellet et al. in view of Acosta et al.

Since rejection of amended base claim 31 over Bellet et al. is being maintained, therefore rejection of amended claim 41 and 42 over Acosta et al. is also being maintained.

Regarding claim 41, Applicant is arguing limitations that are not part of the instant claims.

Bellet et al teach method of claim 31 but do not teach sample is taken from peripheral blood or tissue is taken from endometrium. Acosta et al. teach where sample is taken from peripheral blood or endometrium. The instant claims do not recite a particular method by which endometrial tissue should be collected. Thus cited art is still applicable and the 103(a) rejection is being maintained.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 41 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Currently claim 41 recites ---- The method according to claim 31 wherein the blood sample is taken from peripheral blood and the tissue is taken from tissue of the endometrium or the cervix of a female patient, wherein, based on the detection of

mRNA expression of at least one of β7-hCG, β6-hCG, and β6e-hCG, the receptivity of the endometrium for an embryo in the actual cycle is determined".

Amendment to claim 41 recites a method that does not recite any specific action or step that must be performed or a condition that must be met, so that mRNA detection of at least one of β7-hCG, β6-hCG, and β6e-hCG can be correlated to receptivity of endometrium in actual cycle. The claim in present form does not tell one of ordinary skill in the art under what conditions detection of hCG mRNA can be correlated with endometrial receptivity and under what conditions detection of hCG mRNA can be correlated with endometrial non receptivity.

Currently claim 42 recites---- The method according to claim 31 wherein the blood sample is taken from menstrual blood and, based on the detection of the mRNA expression of at least one of β7-hCG, β6-hCG, and β6e-hCG, in the menstrual blood of the past cycle, the potential of the receptivity of the endometrium for an embryo in the subsequent cycle is determined".

Amendment to claim 42 recites a method that does not recite any specific action or step that must be performed or a condition that must be met, so that mRNA detection of at least one of β7-hCG, β6-hCG, and β6e-hCG can be correlated to the potential of the receptivity of the endometrium for an embryo in the subsequent cycle is determined. The claim in present form do not tell one of ordinary skill in the art under what conditions detection of hCG mRNA can be correlated to the potential of the receptivity of the endometrium for an embryo in the subsequent cycle and under what conditions

detection of hCG mRNA can not be correlated to the potential of the receptivity of the endometrium for an embryo in the subsequent cycle

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 31 is rejected under 35 U.S.C. 102(b) as being anticipated by Bellet et al. (US Pat. 6,194,154 B1 issued Feb 2001 with a PG.Pub date of September 4, 1998).

Regarding claim 31, Bellet et al teaches: a method for determining specific conditions or changes in the endometrium or in the epithelium of other organs, the method comprising the steps of:

a) isolating RNA (see col. 5, lines 35-44 where RNA isolation is taught) from a blood sample or tissue sample (see col. 4, lines 46-53 where wide variety of tissue samples including whole blood are taught); and

b) quantitatively measuring in said blood sample or said tissue sample the expression or over expression of mRNA (see col. 4 line 4 where RT-PCR is taught for expression or over expression of mRNA for detection of CGβ transcripts) of at least one of β7-hCG, β6-hCG, and β6e-hCG (see col. 1, line 43 where β7-hCG and β6-hCG are taught).

Thus all active steps of claim 31 that are the only active steps of the recited claim as currently presented are taught by Bellet et al.

The newly added limitation wherein detection of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG indicates receptivity of the endometrium for implantation does not introduce any active step that distinguishes the claimed invention over prior art. The added limitation is describing how those results namely detection of mRNA is being interpreted.

Hence Bellet et al. teaches all elements of claim 31.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellet et al. as applied to claim 31 above, and further in view of Acosta et al. (April 2000) Fertility and Sterility vol. 73, no. 4 pp 788-798.

Regarding claim 41, Bellet et al. teach method of claim 31. Bellet et al teach whole blood sample.

Regarding claim 41, Bellet et al. do not teach wherein the blood sample is taken from peripheral blood and the tissue sample is taken from tissue of the endometrium or the cervix of a female patient.

Regarding claim 41, Acosta et al. teach wherein the blood sample is taken from peripheral blood and the tissue sample is taken from tissue of endometrium or cervix of a female patient (see page 790 under section Menstrual cycle monitoring par. 3 where peripheral blood sampling is taught and par. 4 where endometrial biopsy sample is taught. This sample is from healthy fertile female volunteer—see page 790 section titled Volunteers par. 1). By teaching collecting endometrial tissue samples from female volunteers, Acosta et al. teach to one of ordinary skill in the art that same technique can be used to collect samples from female patient. Hence Acosta et al. teach wherein the blood sample is taken from peripheral blood and the tissue sample is taken from tissue of endometrium or cervix of a female patient.

Regarding claim 42, Acosta et al. do not specifically teach wherein the blood sample is taken from menstrual blood. However Acosta et al. do teach the method of endometrial dating and determination of the window of implantation in healthy fertile women.

It would have been prima facie obvious to one of ordinary skill in the art to practice the method Acosta et al. in the method of Bellet et al. at the time the invention was made. The motivation to do so is provided by Acosta et al. who explicitly teach

endometrial dating. Also one of ordinary skill in the art knows that menstrual blood contains the cells that are shed from the uterus lining (endometrium) if implantation of an embryo does not occur to establish a pregnancy. (see the overview section of Menstrual Cycle from free encyclopedia provided by Examiner). Thus menstrual blood is a good source of endometrial cells that have been sloughed off from the uterus. Collection of menstrual blood is non invasive, hence it would be obvious to one of ordinary skill in the art to use menstrual blood for obtaining the endometrial cells instead of using peripheral blood (an invasive collection procedure). Use of menstrual blood will result in no discomfort for the patient and will also require no specially trained technician to draw the peripheral blood resulting in a more cost effective method.

Conclusion

13. All claims under consideration 31, 41 and 42 are rejected over prior art.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suchira Pande whose telephone number is 571-272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
12/6/07